Plasma Membrane I

I. Basic Functions of the Plasma Membrane

A. Regulate nutrient and ion transport into the cell

B. Regulate transport of waste out of the cell

C. Maintain correct chemical conditions in the cell

D. Provide a site for lipid-based chemical reactions

E. Interact with other cells or the ECM

F. Detect and transduce signals from environment to cell (signal transduction)

II. Types of Membrane Lipids

A. Two Main Components of the Membrane

1. Lipids

a. Form a permeable barrier

b. Define the basic architecture

2. Proteins

a. Define the unique functions of the membrane

b. Determine what can pass through the membrane

i. Transporters, channels, junctions

c. Energy uptake, signal transduction (through receptors)

B. Lipids

1. Water insoluble, highly soluble in organic solvents (nonpolar structures)

2. Fuel and energy storage (triglycerides)

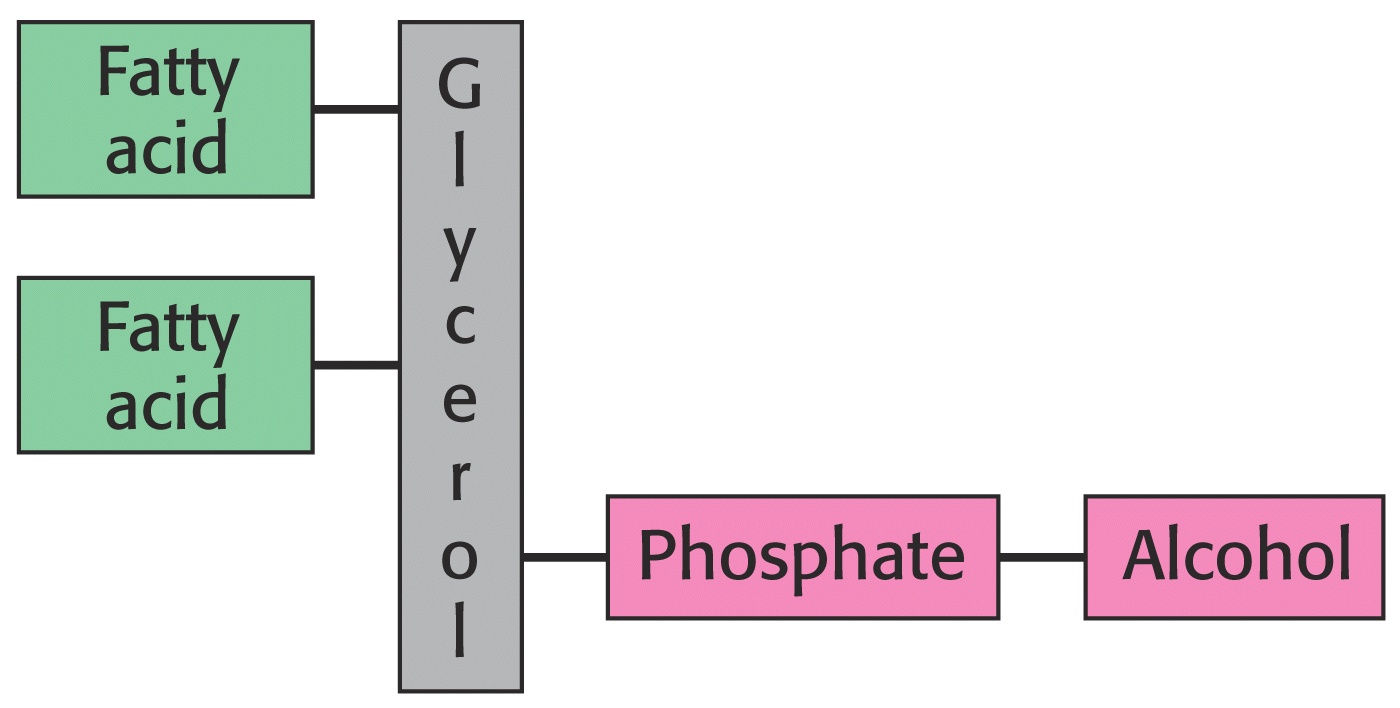
3. Signaling

4. Major membrane components

C. Three Common Types of Membrane Lipids

1.Phospholipids

a. Basic structure



backbone

Hydrophobic

“tail”

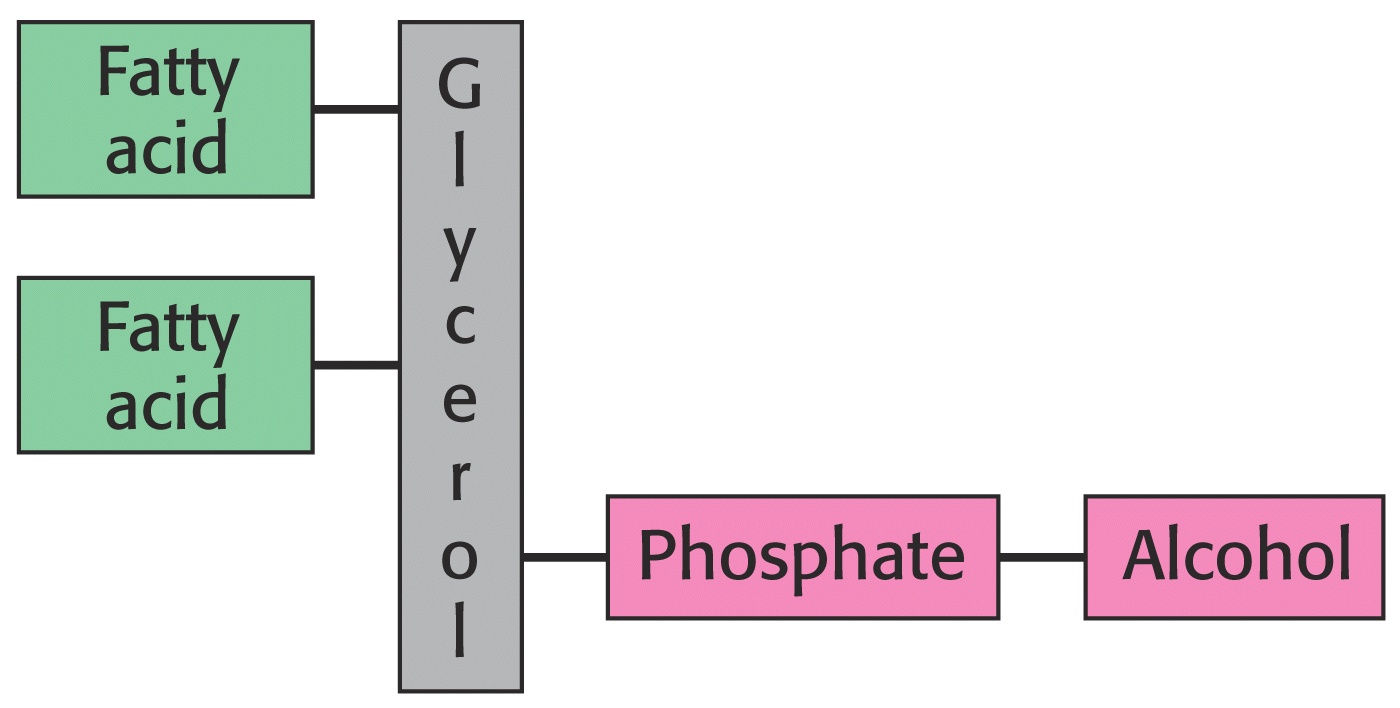
Hydrophilic

“head”

b. Membrane lipids are amphipathic

2. Glycolipids

a. Basic structure



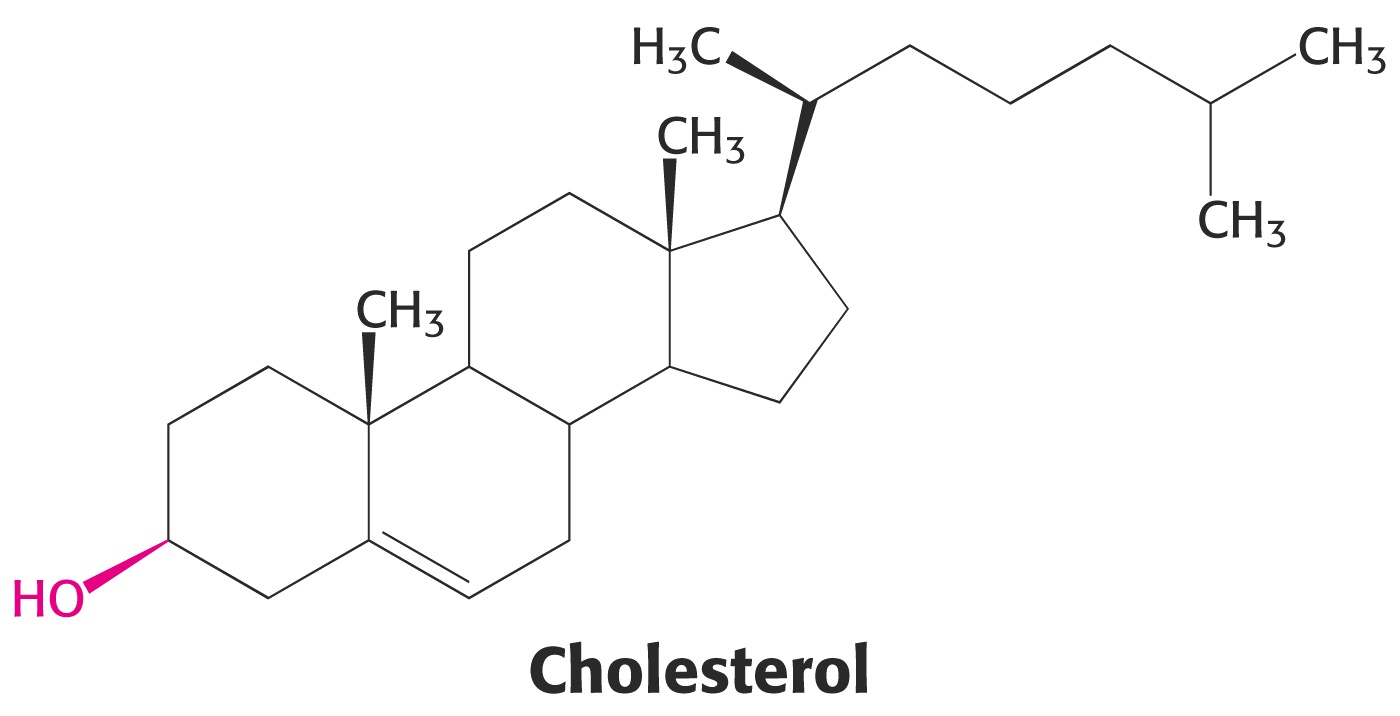
**Sugar**

b. Sugar-containing lipids

c. A sugar takes the place of the phosphate grou

3. Cholesterol

a. Structure



b. 4 linked hydrocarbon rings and hydrocarbon tail (hydrophobic)

c. Alcohol (hydrophilic)

D. Arrangements of Lipids

1. In aqueous media, phospholipids and glycolipids spontaneously form a bilayer

a. Exoplasmic – lipids whose head faces the extracellular environment

b. Cytoplasmic – lipids whose head faces the intracellular environment

2. Two structures that satisfy amphipathic nature of lipids

a. Micelle – Sphere of lipids with all heads facing out and all tails facing center

i. Solubilization of membrane proteins by coating hydrophobic region

b. Liposomes – Spherical lipid bilayer with a cavity in the middle

i. Important for drug delivery and therapeutics

III. Membrane Proteins

A. Selective Permeability

1. Structure of the lipid bilayer prevents most particles from passing through

a. Gases and small, uncharged, polar molecules can pass through diffusion

b. Proteins are required for transport of anything else

i. May be a channel, transporter, pump, etc.

B. Membrane Proteins

1. Carry out most membrane processes

2. Two Classifications

a. Integral – protein that enters or spans the hydrophobic core

i. Tightly associated with the membrane

ii. Removed only by disrupting the membrane (detergents)

b. Peripheral – protein that does not enter the hydrophobic core

i. Loosely associated with the membrane

ii. Removed without disrupting the membrane (salt/pH)

3. Secondary Structures

a. α-helix is a common transmembrane motif in higher organisms

b. Consists of 20-25 AA, rich in hydrophobic residues

c. Transmembrane regions can be predicted from hydropathy plots

3. Lipid Anchors

a. Certain proteins are covalently attached to “lipid anchors”

i. The lipid moieties are what attaches the protein to the membrane

ii. Result of a post-translational modification

C. Studying Membrane Proteins

1. Disruption of membrane with detergents to first remove protein

2. Purified protein is mixed with phospholipids

3. Protein naturally embeds itself within the formed bilayer to fold correctly

4. Results in a liposome with only one type of membrane protein

IV. Membrane Fluidity

A. Importance

1. Influences arrangement of proteins and lipids

2. Foster assembly/disassembly of proteins and signaling complexes in membrane

3. Changes membrane permeability

4. Excessive fluidity leads to membrane destruction

5. Altering fluidity can alter membrane and/or cell function

B. Effects of Fatty Acid Composition

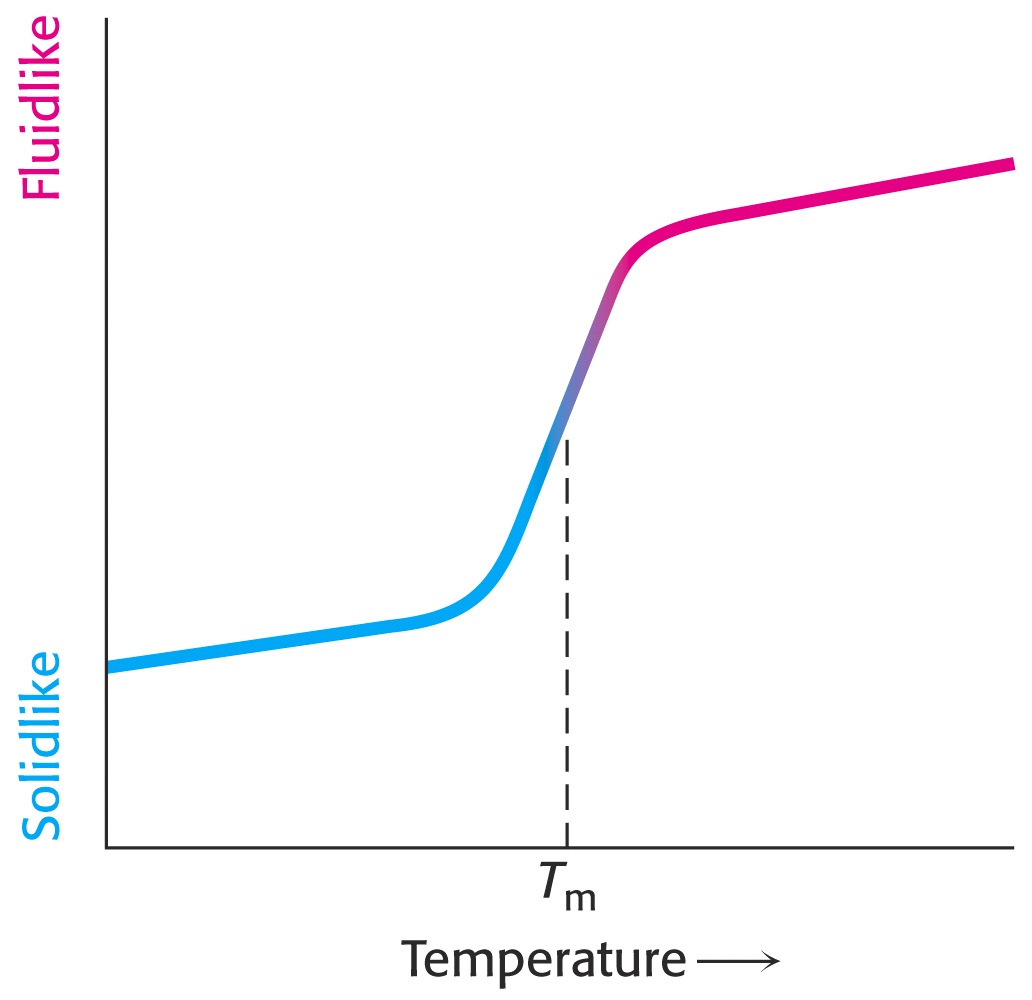
1. Unsaturated FA – contains cis-alkene that introduces a “kink” to the structure

a. Disrupts tight packing of side chains and allows for more fluidity

2. Saturated FA – contains only alkanes

a. Allows tight packing of side chains and causes more rigidity

3. Melting Temperature (Tm)

 a. Phase-transition temperature (heat needed to disrupt the membrane)

b. Curve shifts left (Tm decreases) if characteristics make it more fluid

i. Shorter acyl chain, unsaturated

c. Curve shifts right (Tm increases) if characteristics make it less fluid

i. Longer acyl chain, saturated

4. Cholesterol

a. Disrupts regular side chain interactions

b. Makes membrane less likely to undergo phase transition

c. Cholesterol acts like a fluidity “buffer”

d. If below Tm, cholesterol adds a “kink” to disrupt tight packing

i. Results in increased fluidity

e. If above Tm, cholesterol will limit the free movement due to its planarity

i. Results in decreased fluidity

5. Mobility of Lipids

a. Lateral diffusion of lipids is rapid

b. Rotational diffusion is also rapid

c. Traverse diffusion is very rare due to unfavorable interactions

i. Can occur with the help of ATP-driven flippases and floppases

6. Mobility of Membrane Proteins

a. Depends on several things:

i. Size of protein

ii. Interactions with other molecules

iii. Temperature

iv. Lipid composition of membrane

v. Composition of protein

7. FRAP Method

a. Fluorescence Recovery After Photobleaching

i. A specific protein is tagged with a fluorescent antibody

ii. The antibody will cause the entire membrane to fluoresce

iii. Specific area is bleached with a laser, no longer fluoresces

iv. Color recovery is related to the rate of diffusion of tagged proteins

V. Membrane Asymmetry

A. Asymmetric distribution occurs for membrane proteins and lipids

1. Exoplasmic and cytoplasmic membrane surfaces vary in composition

2. Asymmetry is key to proper function

3. Each cell has unique repertoire of asymmetrically distributed membrane proteins

B. Phosphatidyl Serine (PS)

1. Membrane protein normally found in the cytoplasmic leaflet of RBC

2. Exposure on the exoplasmic leaflet occurs in pathological states

a. Exposed PS causes macrophage recognition and destruction of RBC

b. Cells undergoing apoptosis expose PS to signal macrophages for clean up

C. Topologies of Membrane Proteins

1. Every membrane protein has a specific and consistent topology

2. Topology is determined at the time of synthesis in the ER

a. Does not change, the specific topology is required for function

3. Glycosylation

a. Addition of sugars to a protein, can only occur on the exoplasmic domain

b. Added in the ER and Golgi

c. Can be N-linked (Asn) or O-linked (Ser, Thr)

D. Erythrocytes

1. Functionality is tied tightly to plasma membrane integrity

2. Easy to study because of ease to obtain and the lack of protein synthesis (no nuc)

3. Several important membrane proteins:

a. Akyrin (peripheral)

b. Glycophorin (integral)

4. Hereditary Spherocytosis

a. Mutations in ankyrin, spectrin, or other membrane protein genes

b. Leads to a weakened plasma membrane 🡪 cell becomes prone to lysis